PATENT
CUSTOMER No. 32425

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Johan FROSTEGARD	Group Art Unit: 1641
Serial No.: 10/814,194	Examiner: LISA V. COOK
Filed: April 1, 2004	Atty. Dkt. No.: EPCL:011US
For: METHOD OF DIAGNOSING SPONTANEOUS ABORTION	

CERTIFICATE OF ELECTRONIC SUBMISSION

DATE OF SUBMISSION: December 18, 2006

DECLARATION OF DR. FROSTEGÅRD UNDER 37 C.F.R. §1.132

I, Johan Frostegård, do declare that:

1. I am a citizen of Sweden residing at De Geersgatan 16, SE-115 29 Nacka, Sweden. I currently hold the position of Professor of Medicine and Senior Consultant in Rheumatology at the Karolinska University Hospital Huddinge, Sweden. I am the inventor of the above-captioned application and co-founder, co-owner and a member of the Board of Directors of Athera Biotechnologies AB, the assignee of the above patent application.

2. I earned an M.D. 1987, and a Ph.D. 1992. My research experience includes clinical work with patients in the field of Rheumatology, especially with Systemic lupus erythematosus (SLE), where presence of autoantibodies is a common condition which of needs to be treated. I am

therefore very familiar with the role and evaluation of such antibodies, including antiphospholipid antibodies.

3. I am familiar with the subject matter of the above-captioned application and I reviewed the specification as filed, the claims as presented for reconsideration, the most recent office action and the Muzya *et al.* reference cited therein.

4. In clinical immunology, determination of anti-phospholipid antibodies (aPL) is of great importance in some autoimmune diseases, most notably SLE and antiphospholipid antibody syndrome. Having such antibodies in this field always means having very high levels, typically above 2 standard deviations of controls, and often even higher. Lower levels of antibodies are considered negative, e.g., these patients are judged not to have the syndrome/disease/antibodies if the observed levels are below this limit. aPL include antibodies against cardiolipin, β2GPI, phosphatidylserine, phosphatidylcholine and prothrombine.

5. The Muzya reference concerns anti-phospholipid antibodies, and more specifically, anti-phosphatidylcholine antibodies. As stated in Muzya, "The aim of this study was to investigate the reaction of blood serum containing antiphosphatidylcholine antibodies with PAF and its structural analogues." Apparently, Muzya is limited to a study of blood sera containing phosphatidylcholine antibodies as their aim was to study how these phosphatidylcholine antibodies cross-react with PAF and PAF analogues. These blood sera were taken from patients presenting with obstetric and gynaecological pathologies.

6. By pre-selecting blood sera containing phosphatidylcholine antibodies, the results presented by Muzya is relevant for their stated goal – determining the level of cross-reactivity of the antibodies present in these sera, no more and no less. However, because that these blood sera apparently were pre-selected for anti-phosphatidylcholine antibodies, the ability of such antibodies to cross-react with PAF and certain PAF analogues must be viewed in isolation. In other words, one cannot assume that the mere presence of cross-reactive anti-PAF antibodies would mean that there were sufficient levels to establish, on their own, an increased risk of spontaneous abortion. Indeed, the conclusion made by Muzya is "Antiphosphatidylcholine antibodies in the blood serum of patients with an obstetric and gynaecological pathology bind *in vitro* with phospholipid PAF, PAF lysine derivatives and PAF acyl analogues." However, notably, Muzya makes no suggestion that antibodies to PAF can ***themselves*** be used as a diagnostic tool for gynecologic disorders.

7. I declare that all statements made herein of my own knowledge are true, and that all statements of my own belief are believed to be true, and further that these statements were made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under § 1001 of title 18 of the United States Code.

18 Dec 2006
Date

Johan Frostegård, MD, Ph.D.